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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,146	01/17/2002	Bernhard Hauer	50915	6323

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Keil & Weinkauf
1350 Connecticut Avenue NW
Washington, DC 20036

EXAMINER

PAK, YONG D

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 08/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/031,146

Applicant(s)

HAUER ET AL.

Examiner

Yong D Pak

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 May 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14 and 16-24 is/are pending in the application.
- 4a) Of the above claim(s) 1-8, 13-14, 16 and 19-24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 9-12, 17 and 18 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>7 & 8</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The response filed on May 20, 2004 has been entered. This application is 371 of PCT/EP00/07253.

Claims 1-14 and 16-24 are pending.

Election/Restrictions

Applicant's election with traverse of Group III in Paper No. 10 is acknowledged. The traversal is on the ground(s) that a special technical feature links Groups I-IV. Applicants argue that Munro et al. do not teach mutant monooxygenases having modified substrate specificity, the special technical feature. This is not found persuasive because the mutant monooxygenases of Munro et al. inherently possesses modified substrate specificity. It is very well established in the art that modification of at least one amino acid imparts modified substrate specificity since the structure of a protein denotes its function. Therefore, the substrate specificity of the various mutants of Munro et al. are different from the specificity of its wildtype.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-8, 13-14, 16 and 19-24 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10.

Claim Rejections - 35 USC § 112

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The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11-12 and 17-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 11-12, "Bacillus megaterium" should be italicized because the scientific names of organisms are italicized.

In claim 12, clauses b) and c), a conjunction is missing. It is unclear if the mutations are in the alternative.

Claims 17-18 recite the limitation " at least one compound selected from the groups a) to d) of compounds defined above " in lines 1-2. There is insufficient antecedent basis for this limitation in the claim.

Claims 9-12 and 17-18 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: steps of converting non-heterocyclic aromatic substrates into heterocyclic aromatic compounds. The methods only recite steps of oxidizing heterocyclic aromatic compounds.

Claim Rejections - 35 USC § 102

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The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 9-10 and 17-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Wong et al.

Wong et al. (form PTO-1449 – GB 2 06 485 A) teach a method of oxidizing N- or S-heterocyclic mono- or polynuclear aromatic compounds with a P450_{CAM}, cytochrome P450 monooxygenase from *Pseudomonas putida* (pages 2-3, 7-9 and 13-31). The method of Wong et al. is carried out at a temperature of about 20-40°C, a pH of about 6-9 and a reaction medium containing about 10-100 fold molar excess of the substrate (pages 10-11). Therefore, the teachings of Wong et al. anticipate claims 9-10 and 17-18.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 9 and 11-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wong et al. in view of Graham-Lorence et al.

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Wong et al. teach a method of oxidizing N- or S-heterocyclic mono- or polynuclear aromatic compounds with a P450_{CAM}, as discussed above. Wong et al. also teach that replacement of any aromatic residues in the active site with a smaller, hydrophobic non-aromatic side-chain provides an "aromatic pocket" which could bind more hydrophobic substrates (page 3).

The difference between the reference of Wong et al. and the instant invention is that the reference of Wong et al. does not teach a method of oxidizing heterocyclic aromatic compounds using mutant P450 BM-3, cytochrome P450 monooxygenases from *Bacillus megaterium*.

Graham-Lorence et al. (form PTO-1449) teach a mutant P450 BM-3 having a Val residue at position 87 of SEQ ID NO:2 (abstract). Phe-87 lies in the binding pocket and substitution of the residue with a non-aromatic hydrophobic residue Val provides an "aromatic pocket" which could bind more hydrophobic substrates, similar to the mutant of Wong et al. Also, since P450 BM-3 is very well known and its structure and function are well characterized in the art, it is a good model in understanding substrate specificity of P450s (page 1127).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to use the mutant P450 BM-3 of Graham-Lorence et al. to oxidize heterocyclic aromatic compounds. The motivation of using the mutant of Graham-Lorence et al. is out of convenience since the enzyme is well known and well characterized in the art and the two enzymes are homologous. One of

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skill in the art would have had a reasonable expectation of success since the mutants of both Wong et al. and Graham-Lorence have an "aromatic pocket".

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 703-308-9363. The examiner can normally be reached on 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Yong D. Pak
Patent Examiner



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